Synthesis, properties, and structures of ammonium 4-aryl-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates

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The reaction of arylcyanomethylenethioacetamides with Meldrum acid gave Michael adducts as ammonium salts. When heated in alcohol, these salts undergo cyclization to ammonium 4-aryl-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates. The structure of *N*-methylmorpholinium 4-(2′-chlorophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate was established by X-ray structural analysis.

Key words: arylmethylenecyanothioacetamides, Meldrum acid, reaction, cyclization; ammonium 4-aryl-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates, alkylation, rearrangement; *N*-methylmorpholinium 4-(2′-chlorophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolate, X-ray structural analysis.

Meldrum acid and its derivatives are successfully used in the synthesis of substituted tetrahydropyridin-2-ones,[1,2] octahydroquinoline-2,5-diones,[3] and azepin-3(2*H*)-ones,[4] as well as of isotopically labeled [5-^{14}C]-tetrahydropyridines. The last-mentioned compounds are used in studies of absorption, biodistribution, and metabolism and for isolation of dihydropyridines, which exhibit hypotensive activity.[5] The use of Meldrum acid is based on the ability of the 1,3-dioxanedione fragment to open the ring under the action of various nucleophiles with elimination of acetone and carbon dioxide and formation of carbonyl-containing heterocycles.[3] Meldrum acid and its derivatives, which are, undoubtedly, promising synthons, were not previously used in the synthesis of sulfur analogs of the above-mentioned classes of compounds, although an unsuccessful attempt was made.[6]

In this work, we studied heterocyclization of Michael adducts obtained by the reaction of Meldrum acid (**1**) with arylmethylenecyanoacetamides (**2**) (Scheme 1). Boiling of adducts **3** in alcohol afforded ammonium 4-aryl-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates (**4**) in yields of 61—85%. This reaction also proceeds in benzene, but yields of the target products were lower (30%).

Salts **4** give sulfides **6** under the action of halides **5** (see Scheme 1). When this reaction was carried out with the use of ω-bromoacetyl-2-thiophene as an alkylating agent, substituted 4,5,6,7-tetrahydrothieno-[2,3-*b*]pyridines (**7**) were obtained. Because 6-(alkylthio)tetrahydropyridinones **6** formally have two nucleophilic centers (the NH group and the fragment of the pyridine nucleus, which can undergo enolization $-CH_2-C(O)- \rightleftharpoons -CH=C(OH)-$), it was reasonable to study their reactions with halides **5**. Using the reaction of 4-(4′-bromophenyl)-5-cyano-6-methylthio-3,4-dihydropyridin-2(1*H*)-one (**6l**) with iodomethane in DMF in the presence of an aqueous KOH solution as an example, it was demonstrated that alkylation of compounds **6** proceeds regioselectively at the N atom to form tetrahydropyridin-2-ones **8**.

When heated in benzene, compound **6a** underwent regioselective [3,3]-sigmatropic rearrangement[7] to substituted piperidine **9**. The above-mentioned rearrangement was observed in this series for the first time.[8—10]

The data from NMR and IR spectroscopy confirmed the structures of compounds **4** and **6—9** (Tables 1 and 2, see Experimental).

With the aim of revealing the direction of heterocyclization of Michael adducts **3** and establishing the structures of its products, compound **4a** was studied by X-ray structural analysis. The overall view of the cation and the anion is shown in Fig. 1. The bond lengths and bond angles in molecule **4a** are given in Tables 3 and 4, respectively.

In the anion of the salt under study, the conformation of hydrogenated heterocycle can be described as a

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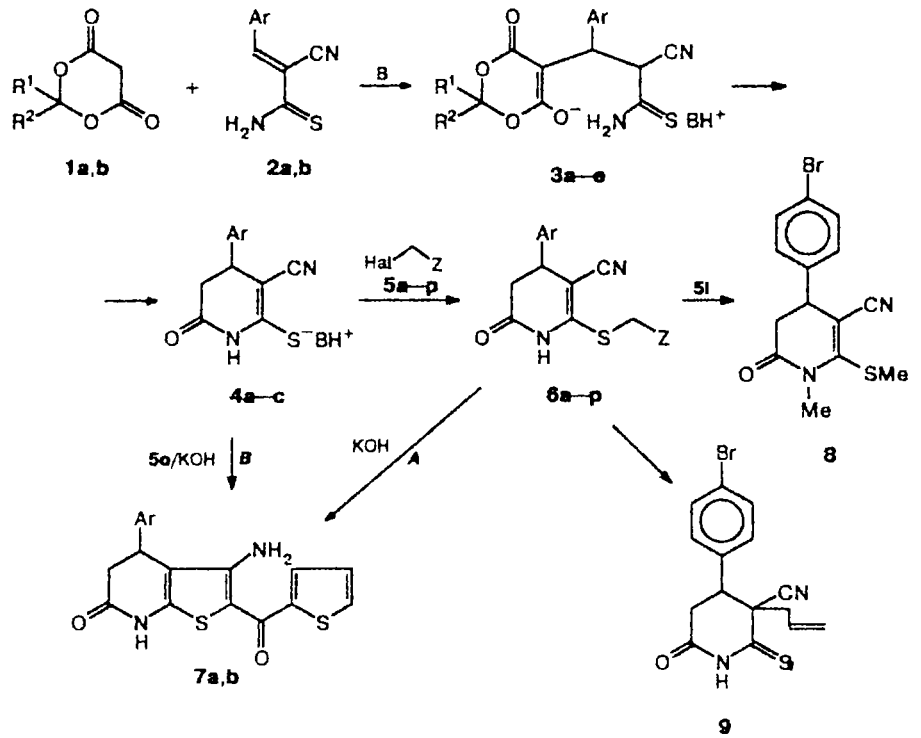
Scheme 1



1a,b **2a,b** **3a–e** **4a–c** **6a–p** **7a,b** **8** **9**

1: $R^1 = R^2 = Me$ (**a**); $R^1–R^2 = (CH_2)_5$ (**b**)
2, 7: Ar = 2-ClC_6H_4 (**a**); 4-BrC_6H_4 (**b**)

3, 4	Ar	$R^1 = R^2$ or $–R^1–R^2–$	B
3a	2-ClC_6H_4	Me	*N*-Methylmorpholine
3b	2-ClC_6H_4	$–(CH_2)_5–$	*N*-Methylmorpholine
3c	4-BrC_6H_4	Me	*N*-Methylmorpholine
3d	4-BrC_6H_4	$–(CH_2)_5–$	*N*-Methylmorpholine
3e	4-BrC_6H_4	Me	Piperidine
4a	2-ClC_6H_4	—	*N*-Methylmorpholine
4b	4-BrC_6H_4	—	*N*-Methylmorpholine
4c	4-BrC_6H_4	—	Piperidine

5, 6	Hal	Z	Ar
a	Br	$CH=CH_2$	4-BrC_6H_4
b	I	Me	4-BrC_6H_4
c	Br	4-BrC_6H_4CO	4-BrC_6H_4
d	Br	Et	4-BrC_6H_4
e	Br	$(CH_2)_3Br$	4-BrC_6H_4
f	Cl	Ph	4-BrC_6H_4
g	Cl	$CONH_2$	4-BrC_6H_4
h	Cl	PhNHCO	4-BrC_6H_4
i	Cl	COOEt	4-BrC_6H_4
k	Cl	4-BrC_6H_4NHCO	4-BrC_6H_4
l	I	H	4-BrC_6H_4
m	I	H	2-ClC_6H_4
n	I	Me	2-ClC_6H_4
o	Br	Thenoyl	2-ClC_6H_4
p	Br	Thenoyl	4-BrC_6H_4

distorted half-chair with the C(4) and C(5) atoms deviating from the plane through the remaining four atoms of the ring (planar to within ±0.039 Å) by 0.347 and −0.283 Å, respectively. Previously,[11] an analogous conformation of this heterocycle was observed for 5-cyano-3-ethoxycarbonyl-4-(2′-iodophenyl)-6-methoxycarbonylmethylthio-3,4-dihydropyridin-2(1*H*)-one containing bulky substituents. The dihedral angle between the pseudoaxial *o*-chlorophenyl ring and the planar fragment of the heterocycle is 85.9°. Such a position of the substituent results in the minimum number of intramolecular steric nonbonded contacts: Cl(1)...C(4), Cl(1)...C(5), and Cl(1)...H(4) are 3.055(2), 3.347(2), and 2.70(2) Å, respectively (the sum of the van der Walls radii of the Cl and C atoms is 3.45 Å, and the sum of the van der Walls radii of the Cl and H is 2.95 Å[12]), which hinders its rotation about the C(4)—C(8) bond. The C(4)—C(8)—C(9)—Cl(1) and H(4)—C(4)—C(8)—C(9) torsion angles (−3.3° and 42.5°, respectively) are indicative of a synperiplanar orientation of the aryl fragment with respect to the H atom at the C(4) atom (see Fig. 1).

In the anion, the negative charge is formally located on the S atom, which is confirmed by the C(2)—S(1) bond length [1.721(1) Å]. This length coincides with the corresponding values observed in analogous salts of hydrogenated pyridines.[13,14] In the almost planar S(1)—C(2)=C(3)—C(7)≡N(2) fragment, conjugation ap-

Table 1. Yields, melting points, and the data of elemental analysis of compounds **6a—p**

Compound	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)					Molecular formula
			C	H	Hal	N	S	
6a	71	153—155 (EtOH)	51.40 / 51.59	3.82 / 3.75	22.94 / 22.88	7.89 / 8.02	9.02 / 9.18	$C_{15}H_{13}BrN_2OS$
6b	76	178—179 (EtOH)	49.71 / 49.86	3.95 / 3.89	23.78 / 23.69	8.15 / 8.31	9.34 / 9.51	$C_{14}H_{13}BrN_2OS$
6c	83	137—139 (AcOH—EtOH, 1 : 3)	47.29 / 47.45	2.84 / 2.79	31.71 / 31.57	5.42 / 5.53	6.10 / 6.33	$C_{20}H_{14}Br_2N_2O_2S$
6d	71	134—136 (EtOH)	51.42 / 51.29	4.11 / 4.30	22.58 / 22.75	8.14 / 7.98	9.01 / 9.13	$C_{15}H_{15}BrN_2OS$
6e	65	155—157 (EtOH)	43.02 / 43.26	3.48 / 3.63	36.14 / 35.98	6.50 / 6.31	7.10 / 7.22	$C_{16}H_{16}Br_2N_2OS$
6f	81	158—160 (EtOH)	57.00 / 57.15	3.83 / 3.79	20.18 / 20.01	6.90 / 7.02	7.84 / 8.03	$C_{19}H_{15}BrN_2OS$
6g	81	203—205 (EtOH)	46.14 / 45.91	3.50 / 3.30	21.63 / 21.82	11.32 / 11.47	8.59 / 8.75	$C_{14}H_{12}BrN_3O_2S$
6h	79	232—234 (AcOH)	54.14 / 54.31	3.74 / 3.65	17.89 / 18.06	9.69 / 9.50	7.11 / 7.25	$C_{20}H_{16}BrN_3O_2S$
6i	57	123—125 (EtOH)	48.78 / 48.62	3.64 / 3.83	20.05 / 20.21	7.23 / 7.09	8.03 / 8.11	$C_{16}H_{15}BrN_2O_3S$
6k	88	217—219 (AcOH)	45.88 / 46.09	3.03 / 2.90	30.72 / 30.66	7.88 / 8.06	6.32 / 6.15	$C_{20}H_{15}Br_2N_3O_2S$
6l	83	225—227 (AcOH—EtOH, 1 : 3)	48.15 / 48.31	3.22 / 3.43	24.89 / 24.72	8.73 / 8.67	9.74 / 9.92	$C_{13}H_{11}BrN_2OS$
6m	80	162—164 (EtOH)	56.20 / 56.01	4.14 / 3.98	12.58 / 12.72	9.88 / 10.05	11.73 / 11.50	$C_{13}H_{11}ClN_2OS$
6n	82	166—168 (EtOH)	57.28 / 57.43	4.30 / 4.48	11.95 / 12.11	9.47 / 9.57	11.11 / 10.95	$C_{14}H_{13}ClN_2OS$
6o	85	180—181 (EtOH)	55.31 / 55.59	3.12 / 3.37	8.90 / 9.12	7.41 / 7.20	16.55 / 16.49	$C_{18}H_{13}ClN_2O_2S_2$
6p	77	209—210 (BuOH—DMF, 1 : 1)	49.72 / 49.89	2.84 / 3.02	18.53 / 18.44	6.60 / 6.46	14.58 / 14.80	$C_{18}H_{13}BrN_2O_2S_2$

parently leads to a slight shortening of single bonds and elongation of double bonds, which was also noted previously.[13,14]

The *N*-methylmorpholinium cation adopts a chair conformation. The O(2) and N(3) atoms deviate from the plane through the remaining four atoms (the average deviation of the atoms is +0.003 Å) by −0.676 and 0.628 Å, respectively. The cation as a whole has an ordinary structure.[14,15]

In the crystal, anions and cations are linked to each other through intermolecular N(3)—H(3)...S(1) (x, y, z) hydrogen bonds [N(3)...S(1), N(3)—H(3), and H(3)...S(1) are 3.175(2), 0.87(2), and 2.34(2) Å, respectively, and the N(3)—H(3)...S(1) angle is 161(1)°]. The H atom at N(1) is not involved in hydrogen bonding [the intermolecular van der Waals H(1)...S(1) contact ($1 - x$, $1 - y$, $1 - z$) is 2.81(2) Å].

Experimental

The IR spectra were obtained on an IKS-29 spectrophotometer as Nujol mulls. The ^{1}H NMR spectrum was recorded on a Bruker WP-100 SY instrument (100 MHz) in DMSO-d_6 relative to $SiMe_4$. The identities of the compounds were monitored by TLC on Silufol UV-254 plates in an acetone—heptane system (3 : 5).

Ammonium 5-(1-aryl-2-cyanoethyl-2-thiocarbamoyl)-2-R^1-2-R^2-6-oxo-1,3-dioxacyclohex-4-ene-4-olates (3a—e) were prepared by the reaction of arylmethylenecyanothioacetamides **2** with Meldrum's acids **1** in the presence of amines according to the known procedure.[6]

***N*-Methylmorpholinium 5-[1-(2′-chlorophenyl)-2-cyano-2-thiocarbamoylethyl]-2,2-dimethyl-6-oxo-1,3-dioxacyclohex-4-ene-4-olate (3a).** The yield was 4.0 g (85%), m.p. 145—147 °C. Found (%): C, 54.12; H, 5.79; Cl, 7.40; N, 8.71; S, 6.99. $C_{21}H_{26}ClN_3O_5S$. Calculated (%): C, 53.90; H, 5.60; Cl, 7.58; N, 8.98; S, 6.85. IR, ν/cm^{-1}: 2220 (C≡N); 1710

Table 2. Spectral parameters of compounds **6a—p**

Compound	IR, ν/cm^{-1}			^{1}H NMR, δ					
	NH	C≡N	NHCO	NH (s)	Ar	H(4) (t)	SCH_2	$CH(3)_2$ (m)	Z
6a	3200	2212	1660	10.63	7.56, 7.17 (both d)	4.03	3.72 (d)	2.25—3.10	5.82 (m, 1 H, CH=); 5.16 (m, 2 H, CH_2=)
6b	3185	2210	1700	10.61	5.54, 7.19 (both d)	4.03	3.00 (m)	2.50—2.95	1.21 (t, 3 H, CH_3)
6c	3360	2210	1715	10.62	7.25—7.90 (m)*	4.07	4.81 (s)	2.65—3.49	7.25—7.90 (m, 4 H, C_6H_4)*
6d	3180	2218	1674	10.63	7.58, 7.17 (both d)	4.03	3.00 (m)	2.50—2.95	1.58 (m, 2 H, CH_2); 0.96 (t, 3 H, CH_3)
6e	3210	2190	1692	10.65	7.57, 7.17 (both d)	4.05	3.35 (t)	2.75—2.95	3.07 (t, 2 H, CH_2Br); 1.78 (m, 4 H, $(CH_2)_2$)
6f	3150	2205	1680	10.79	7.48, 6.92 (both d)	3.93	4.33 (s)	2.25—2.90	7.33 (m, 5 H, C_6H_5)
6g	3150	2220	1700	**	5.50, 7.21 (both d)	4.07	3.79 (s)	2.59—3.10	7.92, 7.60 (both br.s, 2 H, NH_2)
6h	3340	2222	1685; 1720	10.85	7.00—7.70 (m)*	4.08	4.03 (s)	2.61—2.95	10.46 (s, 1 H, NH); 7.00—7.70 (m, 5 H, C_6H_5)*
6i	3150	2205	1680	10.68	7.58, 7.21 (both d)	4.13	4.01 (m)*	2.60—3.10	1.20 (t, 3 H, CH_3); 4.01 (m, 2 H, OCH_2)*
6k	3310	2222	1680; 1710	10.76	7.10—7.65*	4.62	3.98 (d)	2.60—3.00	10.50 (s, 1 H, NH); 7.10—7.65 (m, 4 H, C_6H_4)*
6l	3210	2218	1695	10.57	7.57, 7.17 (both d)	4.04	2.54 (s)	2.65—3.10	—
6m	3200	2195	1684	10.66	7.20—7.65 (m)	4.38	2.60 (s)	2.65—3.20	—
6n	3185	2218	1685	10.70	7.10—7.55 (m)	4.39	3.06 (q)	2.60—2.95	1.27 (t, 3 H, CH_3)
6o	3150	2205	1695	10.73	7.10—7.60 (m)*	4.37	4.74 (s)	2.55—3.10	8.06 (m, 2 H, thienyl); 7.10 (m, 1 H, thienyl)*
6p	3185	2202	1668	10.66	7.56, 7.16 (both d)	4.06	4.70 (s)	2.55—3.00	8.08 (m, 2 H, thienyl); 7.29 (m, 1 H, thienyl)

* The signals overlap. ** No signal is observed, apparently due to deuterium exchange.

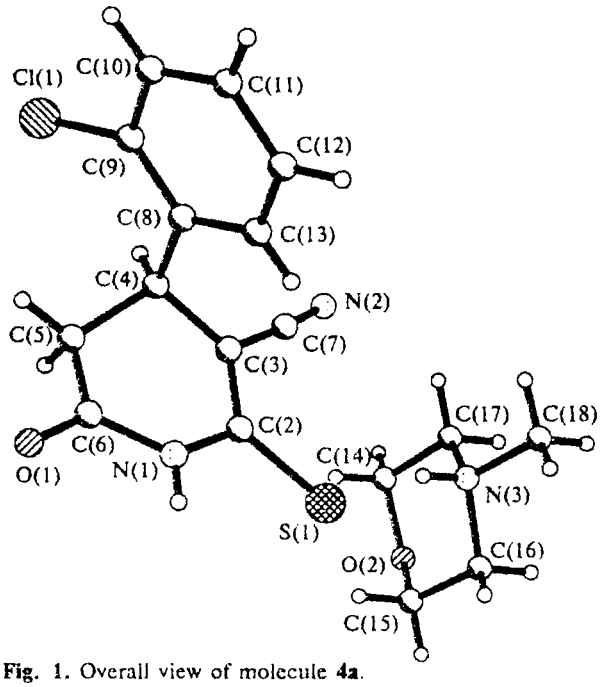


Fig. 1. Overall view of molecule **4a**.

(C=O). ^{1}H NMR, δ: 9.53 (s, 2 H, NH_2); 7.85 (m, 2 H, C_6H_4); 7.15 (m, 2 H, C_6H_4); 5.43 (d, 1 H, CHCN, $^3J_{H(2)-H(1)}$ = 12 Hz); 5.08 (d, 1 H, CHAr, $^3J_{H(1)-H(2)}$ = 12 Hz); 3.77 (m, 4 H, CH_2OCH_2); 3.13 (m, 4 H, CH_2NCH_2); 2.76 (s, 3 H, NCH_3); 1.39 (s, 6 H, 2 CH_3).

***N*-Methylmorpholinium 5-[1-(2′-chlorophenyl)-2-cyano-2-thiocarbamoylethyl]-6-oxospiro[cyclohexane-1′,2-(1,3-dioxacyclohex-4-ene)]-4-olate (3b).** The yield was 4.37 g (86%), m.p. 144—147 °C. Found (%): C, 56.58; H, 6.08; Cl, 7.19; N, 8.00; S, 6.12. $C_{24}H_{30}ClN_3O_5S$. Calculated (%): C, 56.74; H, 5.95; Cl, 6.98; N, 8.27; S, 6.31. IR, ν/cm^{-1}: 3135, 3270, 3400 (NH_2); 2248 (C≡N). ^{1}H NMR, δ: 9.56 (d, 2 H, NH_2); 7.93 (m, 2 H, Ar); 7.16 (m, 2 H, Ar); 5.42 (d, 1 H, CHCN, $^3J_{H(2)-H(1)}$ = 12 Hz); 5.09 (d, CH, CHAr, $^3J_{H(1)-H(2)}$ = 12 Hz); 3.78 (m, 4 H, CH_2OCH_2); 3.15 (m, 4 H, CH_2NCH_2); 2.77 (s, 3 H, NCH_3); 1.69 (m, 4 H, $(CH_2)_2$); 1.38 (m, 6 H, $(CH_2)_3$).

***N*-Methylmorpholinium 5-[1-(4′-bromophenyl)-2-cyano-2-thiocarbamoylethyl]-2,2-dimethyl-6-oxo-1,3-dioxacyclohex-4-ene-4-olate (3c).** The yield was 4.61 g (90%), m.p. 162—164 °C. Found (%): C, 49.11; H, 5.00; Br, 15.70; N, 8.35; S, 6.08. $C_{21}H_{26}BrN_3O_5S$. Calculated (%): C, 49.22; H, 5.11; Br, 15.59; N, 8.20; S, 6.26. ^{1}H NMR, δ: 9.57 (br.s, 2 H, NH_2); 7.43 (m, 4 H, Ar); 4.43 (d, 1 H, CHCN, $^3J_{H(2)-H(1)}$ = 12 Hz); 4.58, 4.40 (both d, 1 H, CHAr, $^3J_{H(1)-H(2)}$ = 12 Hz); 3.77 (m,

Table 3. Bond lengths (*d*) in molecule **4a**

Bond	*d*/Å	Bond	*d*/Å	Bond	*d*/Å	Bond	*d*/Å
Cl(1)—C(9)	1.745(2)	N(1)—C(6)	1.366(2)	C(3)—C(7)	1.414(2)	C(10)—C(11)	1.376(3)
S(1)—C(2)	1.721(1)	N(2)—C(7)	1.147(2)	C(4)—C(5)	1.530(2)	C(11)—C(12)	1.376(3)
O(1)—C(6)	1.216(2)	N(3)—C(16)	1.496(2)	C(4)—C(8)	1.527(2)	C(12)—C(13)	1.392(3)
O(2)—C(14)	1.422(3)	N(3)—C(17)	1.493(2)	C(5)—C(6)	1.498(2)	C(14)—C(17)	1.501(3)
O(2)—C(15)	1.425(3)	N(3)—C(18)	1.487(3)	C(8)—C(9)	1.399(2)	C(15)—C(16)	1.502(3)
N(1)—C(2)	1.401(2)	C(2)—C(3)	1.369(2)	C(8)—C(13)	1.392(2)		
		C(3)—C(4)	1.520(2)	C(9)—C(10)	1.384(2)		

Table 4. Bond angles (ω) in molecule **4a**

Angle	ω/deg	Angle	ω/deg
C(14)—O(2)—C(15)	109.5(2)	N(1)—C(6)—C(5)	115.6(1)
C(2)—N(1)—C(6)	126.1(1)	N(2)—C(7)—C(3)	175.8(2)
C(16)—N(3)—C(17)	110.3(1)	C(4)—C(8)—C(9)	121.1(1)
C(16)—N(3)—C(18)	112.0(2)	C(4)—C(8)—C(13)	122.4(1)
C(17)—N(3)—C(18)	111.3(2)	C(9)—C(8)—C(13)	116.4(1)
S(1)—C(2)—N(1)	114.8(1)	Cl(1)—C(9)—C(8)	119.5(1)
S(1)—C(2)—C(3)	127.8(1)	Cl(1)—C(9)—C(10)	117.9(1)
N(1)—C(2)—C(3)	117.4(1)	C(8)—C(9)—C(10)	122.6(2)
C(2)—C(3)—C(4)	121.2(1)	C(9)—C(10)—C(11)	119.3(2)
C(2)—C(3)—C(7)	120.5(1)	C(10)—C(11)—C(12)	120.1(2)
C(4)—C(3)—C(7)	118.3(1)	C(11)—C(12)—C(13)	120.0(2)
C(3)—C(4)—C(5)	108.8(1)	C(8)—C(13)—C(12)	121.6(1)
C(3)—C(4)—C(8)	113.2(1)	O(2)—C(14)—C(17)	110.9(2)
C(5)—C(4)—C(8)	110.1(1)	O(2)—C(15)—C(16)	111.6(2)
C(4)—C(5)—C(6)	113.6(1)	N(3)—C(16)—C(15)	110.4(2)
O(1)—C(6)—N(1)	121.3(2)	N(3)—C(17)—C(14)	110.7(2)
O(1)—C(6)—C(5)	123.1(1)		

4 H, CH_2OCH_2); 3.16 (m, 4 H, CH_2NCH_2); 2.78 (s, 3 H, NCH_3); 1.45, 1.32 (both s, 6 H, 2 CH_3).

***N*-Methylmorpholinium 5-[1-(4′-bromophenyl)-2-cyano-2-thiocarbamoylethyl]-6-oxospiro[cyclohexane-1′,2-(1,3-dioxacyclohex-4-ene)]-4-olate (3d).** The yield was 4.3 g (78%), m.p. 138—140 °C. Found (%): C, 51.96; H, 5.18; Br, 14.58; N, 7.72; S, 5.71. $C_{24}H_{30}BrN_3O_5S$. Calculated (%): C, 52.18; H, 5.47; Br, 14.46; N, 7.61; S, 5.80. IR, ν/cm^{-1}: 3240 (NH_2); 2240 (C≡N). ^{1}H NMR, δ: 9.57 (br.s, 2 H, NH_2); 7.43 (m, 4 H, Ar); 5.43, 5.30 (both d, 1 H, CHCN, $^3J_{H(2)-H(1)}$ = 12 Hz); 4.57, 4.35 (both d, 1 H, CHAr, $^3J_{H(1)-H(2)}$ = 12 Hz); 3.78 (m, 4 H, CH_2OCH_2); 3.14 (m, 4 H, CH_2NCH_2); 2.77 (s, 3 H, NCH_3); 1.76 (m, 4 H, $(CH_2)_2$); 1.42 (m, 6 H, $(CH_2)_3$).

The melting point and the ^{1}H NMR and IR spectra of compound **3e** obtained were analogous to those reported in the literature.[6]

Ammonium 4-aryl-3-cyano-2-oxo-1,2,3,4-tetrahydropyridine-6-thiolates (4a—c). *A.* A suspension of adduct **3a**, **3c**, or **3e** (10 mmol) in ethanol (20 mL) was refluxed for 3 h. The reaction mixture was cooled. The precipitate was filtered off and washed with ethanol and acetone. ***N*-Methylmorpholinium 4-(2′-chlorophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-2-thiolate (4a).** The yield was 2.67 g (73%), m.p. 163—165 °C. Found (%): C, 55.64; H, 5.73; Cl, 9.80; N, 11.29; S, 8.50. $C_{17}H_{20}ClN_3O_5S$. Calculated (%): C, 55.81; H, 5.51; Cl, 9.69; N, 11.48; S, 8.76. IR, ν/cm^{-1}: 2190 (C≡N); 1675 (C=C). ^{1}H NMR, δ: 8.88 (br.s, 1 H, NH); 7.30 (m, 4 H, Ar); 4.02 (m, 1 H, H(4)); 2.29—2.85 (m, 2 H, CH_2); 3.79 (m, 4 H, CH_2OCH_2); 3.19 (m, 4 H, CH_2NCH_2); 2.80 (s, 3 H, CH_3). ***N*-Methylmorpholinium 4-(4′-bromophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-2-thiolate (4b).** The yield was 3.16 g (77%), m.p. 152—154 °C. Found (%): C, 49.60; H, 4.82; Br, 19.59; N, 10.31; S, 7.65. $C_{17}H_{20}BrN_3O_2S$. Calculated (%): C, 49.76; H, 4.91; Br, 19.47; N, 10.24; S, 7.81. IR, ν/cm^{-1}: 2175 (C≡N); 1690 (C=O). ^{1}H NMR, δ: 8.74 (br.s, 1 H, NH); 7.51 (d, 2 H, Ar); 7.15 (d, 2 H, Ar); 3.79 (m, 4 H, CH_2OCH_2); 3.65 (m, 1 H, H(4)); 3.19 (m, 4 H, CH_2NCH_2); 2.81 (s, 3 H, CH_3); 2.34—2.76 (m, 2 H, CH_2). **Piperidinium 4-(4′-bromophenyl)-5-cyano-2-oxo-1,2,3,4-tetrahydropyridine-2-thiolate (4c).** The yield was 2.4 g (61%), m.p. 179—181 °C. Found (%): C, 51.64; H, 5.23; Br, 20.10; N, 10.48; S, 8.32. $C_{17}H_{20}BrN_3OS$. Calculated (%): C, 51.78; H, 5.11; Br, 20.26; N, 10.66; S, 8.13. IR, ν/cm^{-1}: 2190 (C≡N); 1670 (C=O). ^{1}H NMR, δ: 8.78 (s, 1 H, NH); 7.48 (d, 2 H, Ar); 7.12 (d, 2 H, Ar); 3.64 (m, 1 H, H(4)); 3.00 (m, 4 H, CH_2NCH_2); 2.30—2.72 (m, 2 H, CH_2); 1.56 (m, 6 H, $(CH_2)_3$).

B. A suspension of adduct **3b** or **3d** (10 mmol) in ethanol (20 mL) was refluxed for 3 h. The reaction mixture was cooled. The precipitate was filtered off and washed with ethanol and acetone. Compounds **4a** and **4b** were obtained in yields of 68% and 85%, respectively. The melting points and the ^{1}H NMR spectra of these compounds were analogous to those of the products synthesized by method *A*.

C. A suspension of adduct **3c** (10 mmol) in benzene (20 mL) was refluxed for 3 h. The reaction mixture was cooled. The precipitate was filtered off and washed with ethanol and acetone. The melting point and the data from chromatography for compound **4b** (yield 30%) were analogous to those of the product prepared by method *A*.

4-Aryl-5-cyano-6-*Z*-methylthio-3,4-dihydropyridin-2(1*H*)-ones (6a—p). Halide **5** (10 mmol) was added to a solution of the corresponding salt **4** (10 mmol) in DMF (10 mL). The reaction mixture was stirred at 25 °C for 1.5 h and then diluted with water (15 mL). The precipitate was filtered off and washed with water, ethanol, and hexane. Compounds **6a—p** were obtained (the principal characteristics are given in Tables 1 and 2).

3-Amino-4-(2′-chlorophenyl)-2-thenoyl-4,5,6,7-tetrahydrothieno[2,3-*b*]pyridine (7a). *A.* A 10% aqueous KOH solution (5.6 mL, 10 mmol) was added to a suspension of compound **6o** (10 mmol) in DMF (12 mL). The reaction mixture was stirred for 4 h. The precipitate was filtered off and washed with water, ethanol, and heptane. The yield was 3.11 g (80%), m.p. 282—284 °C (from AcOH). Found (%): C, 55.40; H, 3.14; Cl, 9.31; N, 7.10; S, 16.58. $C_{18}H_{13}ClN_2O_2S_2$. Calculated (%): C, 55.59; H, 3.37; Cl, 9.12; N, 7.20; S, 16.49. IR, ν/cm^{-1}: 3300 (NH_2); 1670 (C=O). ^{1}H NMR, δ: 11.17 (s, 1 H, NH); 7.90 (m, 2 H, thienyl); 7.73 (s, 2 H, NH_2); 7.50 (m, 1 H, thienyl); 7.23 (m, 3 H, Ar); 6.70 (m, 1 H, Ar); 4.63 (d, 1 H, H(4)); 2.62—3.27 (m, 2 H, CH_2).

Table 5. Atomic coordinates ($\times10^4$; $\times10^3$ for H atoms) in molecule **4a**

Atom	x	y	z	Atom	x	y	z	Atom	x	y	z
Cl(1)	−4254(1)	5516(1)	8383(1)	C(10)	−1814(3)	6420(2)	9663(1)	H(11)	14(3)	713(2)	1054(2)
S(1)	4140(1)	6982(1)	4671(1)	C(11)	−105(3)	6949(2)	9872(1)	H(12)	258(3)	761(2)	917(2)
O(1)	2022(2)	3191(1)	7518(1)	C(12)	1339(3)	7228(2)	9051(2)	H(13)	198(3)	717(2)	748(2)
O(2)	2709(2)	9168(1)	749(1)	C(13)	1070(2)	6980(2)	8005(1)	H(141)	94(3)	856(2)	201(2)
N(1)	2763(2)	5070(1)	6288(1)	C(14)	1238(3)	9364(2)	1522(2)	H(142)	3(3)	978(2)	106(2)
N(2)	−801(3)	8911(2)	4358(2)	C(15)	4402(4)	8559(2)	1376(2)	H(151)	401(3)	776(2)	189(2)
N(3)	3775(2)	9682(1)	2833(1)	C(16)	5275(3)	9362(2)	2046(2)	H(152)	531(3)	842(2)	84(2)
C(2)	2290(2)	6288(1)	5579(1)	C(17)	1939(3)	10220(2)	2190(2)	H(161)	570(3)	1017(2)	156(2)
C(3)	462(2)	6794(1)	5698(1)	C(18)	4544(4)	10552(2)	3452(2)	H(162)	635(3)	894(2)	251(2)
C(4)	−925(2)	6116(1)	6638(1)	H(1)	378(3)	477(2)	622(2)	H(171)	231(2)	1102(2)	171(2)
C(5)	−640(3)	4684(2)	6835(1)	H(3)	356(3)	895(2)	333(2)	H(172)	96(3)	1037(2)	274(2)
C(6)	1472(2)	4237(1)	6933(1)	H(4)	−224(2)	633(1)	640(1)	H(181)	570(4)	1018(2)	381(2)
C(7)	−172(2)	7976(2)	4952(1)	H(51)	−134(3)	421(2)	749(2)	H(182)	480(3)	1135(2)	288(2)
C(8)	−638(2)	6449(1)	7759(1)	H(52)	−117(3)	442(2)	623(2)	H(183)	356(4)	1067(2)	398(2)
C(9)	−2060(2)	6175(1)	8620(1)	H(10)	−281(3)	622(2)	1020(2)				

B. ω-Bromoacetyl-2-thiophene (10 mmol) was added to a solution of salt **4a** (10 mmol) in DMF (12 mL), and the reaction mixture was stirred for 30 min. Then a 10% aqueous KOH solution (5.6 mL, 10 mmol) was added, and the reaction mixture was stirred for 2 h. The precipitate was filtered off and washed with water, ethanol, and heptane. Compound **7a** was obtained in a yield of 2.76 g (71%). The melting point and the data from chromatography for compound **7a** were analogous to those of the product synthesized by method *A*.

3-Amino-4-(4′-bromophenyl)-2-thenoyl-4,5,6,7-tetrahydrothieno[2,3-*b*]pyridine (7b) was prepared by method *A* according to a procedure similar to that described above for thienopyridine **7a** using substituted tetrahydropyridinone **6p**. The yield was 3.94 g (91%), m.p. 297—300 °C. Found (%): C, 50.05; H, 2.86; Br, 18.70; N, 6.55; S, 14.61. $C_{18}H_{13}BrN_2O_2S_2$. Calculated (%): C, 49.89; H, 3.02; Br, 18.44; N, 6.46; S, 14.80. IR, ν/cm^{-1}: 1690 (C=O). ^{1}H NMR, δ: 11.10 (s, 1 H, NH); 7.80 (m, 4 H, NH_2, H(4), H(5) of thienyl); 7.51 (d, 2 H, C_6H_4); 7.16 (m, 1 H, H(3) of thienyl); 7.08 (d, 2 H, C_6H_4); 4.41 (d, 1 H, H(4)); 2.58—3.20 (m, 2 H, CH_2).

Compound **7b** was also prepared by method *B* analogously to compound **7a** using salt **4b**. The yield was 2.81 g (65%).

4-(4′-Bromophenyl)-5-cyano-1-methyl-2-methylthio-1,2,3,4-tetrahydropyridin-2-one (8). A 10% aqueous KOH solution (5.6 mL, 10 mmol) was added with stirring to a solution of compound **6l** (10 mmol) in DMF (10 mL). After 1 min, iodomethane (10 mmol) was added. The reaction mass was stirred for 1.5 h and then diluted with water (15 mL). The precipitate was filtered off and washed with water, ethanol, and heptane. The yield was 2.29 g (68%), m.p. 96—98 °C (from EtOH). Found (%): C, 50.00; H, 3.98; Br, 23.51; N, 8.19; S, 9.66. $C_{14}H_{13}BrN_2OS$. Calculated (%): C, 49.86; H, 3.89; Br, 23.69; N, 8.31; S, 9.51. IR, ν/cm^{-1}: 2220 (C≡N); 1700 (C=O). ^{1}H NMR, δ: 7.56 (d, 2 H, C_6H_4); 7.18 (d, 2 H, C_6H_4); 4.00 (t, 1 H, H(4)); 3.29 (s, 3 H, NCH_3); 2.90 (m, 2 H, CH_2); 2.49 (s, 3 H, SCH_3).

3-Allyl-4-(4′-bromophenyl)-3-cyano-6-oxopiperidine-2-thione (9). A suspension of compound **6a** (10 mmol) in benzene (10 mL) was refluxed for 3 h. The reaction mixture was cooled. The precipitate was filtered off and washed with benzene and heptane. The yield was 2.20 g (63%), m.p. 157—159 °C (from EtOH). Found (%): C, 51.72; H, 3.84; Br, 22.60; N, 7.88; S, 9.32. $C_{15}H_{13}BrN_2OS$. Calculated (%): C, 51.59; H, 3.75; Br, 22.88; N, 8.02; S, 9.18. IR, ν/cm^{-1}: 2235 (C≡N); 1695 (C=O). ^{1}H NMR, δ: 13.04 (s, 1 H, NH); 7.60 (d, 2 H, C_6H_4); 7.17 (d, 2 H, C_6H_4); 5.90 (m, 1 H, CH=); 5.38 (m, 2 H, CH_2=); 3.77 (m, 1 H, H(4)); 3.10—3.50 (m, 2 H, CH_2); 2.70—2.95 (m, 2 H, CH_2—CH=).

X-ray structural analysis of compound 4a. Crystals of **4a** are triclinic, at 20 °C a = 6.810(1) Å, b = 10.999(1) Å, c = 12.191(2) Å, α = 73.51(1)°, β = 89.55(1)°, γ = 87.98(1)°, V = 875.0(3) Å^3, d_{calc} = 1.389 g cm^{-3}, Z = 2, space group $P\bar{1}$. The unit cell parameters and intensities of 5056 independent reflections were measured on an automated four-circle Siemens P3/PC diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique to θ_{max} = 28°). The structure was solved by the direct method, which revealed all nonhydrogen atoms, and refined by the full-matrix least-squares method with anisotropic thermal parameters for nonhydrogen atoms using 3614 reflections with $I > 3\sigma(I)$. All hydrogen atoms were located from the difference Fourier syntheses and refined isotropically. The final values of the R factors were as follows: R = 0.034, R_w = 0.034 (S = 0.41). All calculations were carried out using the SHELXTL PLUS program[16] (the PC Version). The atomic coordinates are given in Table 5.

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